

=> d his ful

FILE 'REGISTRY' ENTERED AT 11:46:51 ON 15 JUN 2006  
ACT KHANNA564/A

L1 STR  
L2 44 SEA SSS FUL L1

FILE 'CAPLUS' ENTERED AT 11:47:10 ON 15 JUN 2006

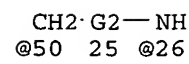
L3 21 SEA ABB=ON PLU=ON L2  
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E E3+AKK  
E E3+ALL  
E E2+ALL  
L4 29091 SEA ABB=ON PLU=ON INTESTINE/OBI (L) DISEASE/OBI OR IBS/OBI  
OR INFLAMMATORY BOWEL/OBI  
L5 6 SEA ABB=ON PLU=ON L4 AND L3  
D SCAN  
L6 12644 SEA ABB=ON PLU=ON COLITIS/OBI OR CROHN#/OBI OR ENTERITIS/OBI  
OR COELIAC/OBI OR ENTERCOLITIS/OBI  
L7 2 SEA ABB=ON PLU=ON L6 AND L3  
L8 6 SEA ABB=ON PLU=ON L7 OR L5  
L9 2 SEA ABB=ON PLU=ON L3 AND 63/SC,SX  
L10 7 SEA ABB=ON PLU=ON L9 OR L8  
L11 44079 SEA ABB=ON PLU=ON G PROTEIN#/OBI  
L12 7 SEA ABB=ON PLU=ON L11 AND L3  
L13 10 SEA ABB=ON PLU=ON L12 OR L10  
D QUE STAT L2  
L14 211 SEA ABB=ON PLU=ON WOODRUFF T?/AU  
L15 316 SEA ABB=ON PLU=ON TAYLOR S/AU  
L16 55 SEA ABB=ON PLU=ON TAYLOR S M?/AU  
L17 113 SEA ABB=ON PLU=ON TAYLOR STEVEN?/AU  
L18 241 SEA ABB=ON PLU=ON FAIRLIE D?/AU  
L19 920 SEA ABB=ON PLU=ON (L14 OR L15 OR L16 OR L17 OR L18)  
L20 9 SEA ABB=ON PLU=ON L19 AND L3  
L21 3 SEA ABB=ON PLU=ON L20 NOT L13  
L22 10 SEA ABB=ON PLU=ON L19 AND L4  
L23 4 SEA ABB=ON PLU=ON L19 AND L6  
L24 10 SEA ABB=ON PLU=ON (L22 OR L23)  
L25 6 SEA ABB=ON PLU=ON L24 NOT (L21 OR L13)  
L26 9 SEA ABB=ON PLU=ON L25 OR L21

FILE 'MEDLINE, BIOSIS' ENTERED AT 12:00:27 ON 15 JUN 2006

L27 0 SEA ABB=ON PLU=ON L2

=> d que stat l2

L1 STR



CH2- CH2- CH2- CH2  
@34 35 36 @37

$$\begin{array}{c}
 48 \\
 \text{O} \\
 \vdots \\
 \text{CH}_2\text{---CH---C---CH---NH} \\
 @42 \quad 43 \quad 44 \quad 45 \quad @46
 \end{array}$$

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 51

claim 1

44 ANSWERS

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FILE COVERS 1907 - 15 Jun 2006 VOL 144 ISS 25  
FILE LAST UPDATED: 14 Jun 2006 (20060614/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>  
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos l13

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L1      STR
L2      44 SEA FILE=REGISTRY SSS FUL L1
L3      21 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L4      29091 SEA FILE=CAPLUS ABB=ON  PLU=ON  INTESTINE/OBI (L) DISEASE/OBI
        OR IBS/OBI OR INFLAMMATORY BOWEL/OBI
L5      6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND L3
L6      12644 SEA FILE=CAPLUS ABB=ON  PLU=ON  COLITIS/OBI OR CROHN#/OBI OR
        ENTERITIS/OBI OR COELIAC/OBI OR ENTERCOLITIS/OBI
L7      2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND L3
L8      6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 OR L5
L9      2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND 63/SC,SX
L10     7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 OR L8
L11     44079 SEA FILE=CAPLUS ABB=ON  PLU=ON  G PROTEIN#/OBI
L12     7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND L3
L13     10 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 OR L10

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=> d que nos l26

*inverted search*

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L1      STR
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L4      29091 SEA FILE=CAPLUS ABB=ON  PLU=ON  INTESTINE/OBI (L) DISEASE/OBI
        OR IBS/OBI OR INFLAMMATORY BOWEL/OBI
L5      6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND L3
L6      12644 SEA FILE=CAPLUS ABB=ON  PLU=ON  COLITIS/OBI OR CROHN#/OBI OR
        ENTERITIS/OBI OR COELIAC/OBI OR ENTERCOLITIS/OBI
L7      2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND L3
L8      6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 OR L5
L9      2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND 63/SC,SX
L10     7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 OR L8
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L18     241 SEA FILE=CAPLUS ABB=ON  PLU=ON  FAIRLIE D?/AU
L19     920 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16 OR L17 OR
        L18)
L20     9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19 AND L3
L21     3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 NOT L13
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L23     4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19 AND L6
L24     10 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L22 OR L23)

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L25 6 SEA FILE=CAPLUS ABB=ON PLU=ON L24 NOT (L21 OR L13)  
 L26 9 SEA FILE=CAPLUS ABB=ON PLU=ON L25 OR L21

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L13 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:700131 CAPLUS

DOCUMENT NUMBER: 143:278782

TITLE: Increased potency of a novel complement factor 5a  
 receptor antagonist in a rat model of  
 inflammatory bowel disease

AUTHOR(S): Woodruff, Trent M.; Pollitt, Sandra; Proctor, Lavinia  
 M.; Stocks, Shelli Z.; Manthey, Helga D.; Williams,  
 Hua M.; Mahadevan, Indumathy B.; Shiels, Ian A.;  
 Taylor, Stephen M.

CORPORATE SOURCE: Promics Pty. Ltd., The University of Queensland,  
 Brisbane, Australia

SOURCE: Journal of Pharmacology and Experimental Therapeutics  
 (2005), 314(2), 811-817

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental  
 Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Aug 2005.

AB We have previously shown that complement factor 5a (C5a) plays a role in  
 the pathogenesis of 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced  
 colitis in rats by using the selective, orally active C5a antagonist  
 AcF-[OP(D-Cha)WR]. This study tested the efficacy and potency of a new  
 C5a antagonist, hydrocinnamate (HC)-[OP(D-Cha)WR], which has limited  
 intestinal luminal metabolism, in this model of colitis. Analogs of  
 AcF-[OP(D-Cha)WR] were examined for their susceptibility to alimentary  
 metabolism in the rat using intestinal mucosal washings. One metabolically  
 stable analog, HC-[OP(D-Cha)WR], was then evaluated pharmacokinetically  
 and investigated at a range of doses (0.03-10 mg/kg/day p.o.) in the 8-day  
 rat TNBS-colitis model, against the comparator drug AcF-[OP(D-Cha)WR].  
 Using various amino acid substitutions, it was determined that the AcF moiety  
 of AcF-[OP(D-Cha)WR] was responsible for the metabolic instability of the  
 compound in intestinal mucosal washings. The analog HC-[OP(D-Cha)WR],  
 equiactive in vitro to AcF-[OP(D-Cha)WR], was resistant to intestinal  
 metabolism, but it displayed similar oral bioavailability to  
 AcF-[OP(D-Cha)WR]. However, in the rat TNBS-colitis model,  
 HC-[OP(D-Cha)WR] was effective at reducing mortality, colon edema, colon  
 macroscopic scores, and increasing food consumption and body wts., at 10-  
 to 30-fold lower oral doses than AcF-[OP(D-Cha)WR]. These studies suggest  
 that resistance to intestinal metabolism by HC-[OP(D-Cha)WR] may result in  
 increased local concns. of the drug in the colon, thus affording efficacy  
 with markedly lower oral doses than AcF-[OP(D-Cha)WR] against  
 TNBS-colitis. This large increase in potency and high efficacy of this  
 compound makes it a potential candidate for clin. development against  
 intestinal diseases such as inflammatory bowel disease.

CC 1-7 (Pharmacology)

IT Complement receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (C5a, antagonists; increased potency of complement factor 5a receptor  
 antagonist in inflammatory bowel disease)

IT Inflammation

Intestine, disease

(colitis; increased potency of complement factor 5a receptor

antagonist in inflammatory bowel disease)

IT Edema  
(colon; increased potency of complement factor 5a receptor antagonist in inflammatory bowel disease)

IT Anti-inflammatory agents  
Body weight  
Feeding  
Gastrointestinal agents  
Human  
(increased potency of complement factor 5a receptor antagonist in inflammatory bowel disease)

IT Intestine, disease  
(inflammatory; increased potency of complement factor 5a receptor antagonist in inflammatory bowel disease)

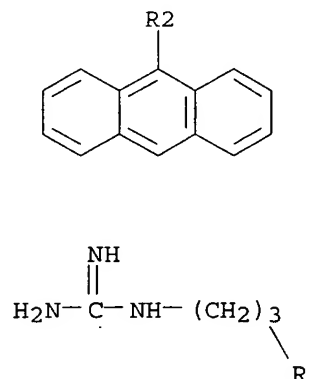
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864238-17-5 864238-18-6 864238-19-7  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(increased potency of complement factor 5a receptor antagonist in inflammatory bowel disease)

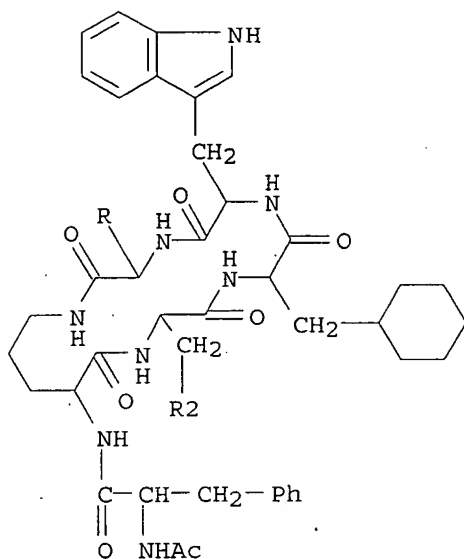
IT 864238-15-3  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(increased potency of complement factor 5a receptor antagonist in inflammatory bowel disease)

RN 864238-15-3 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-3-(9-anthracenyl)-L-alanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI). (CA INDEX NAME)

PAGE 1-A





REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:50809 CAPLUS

DOCUMENT NUMBER: 142:156325

TITLE: Synthesis and evaluation of cyclic oligopeptide analogs as C5a receptor antagonists for treatment of disease

INVENTOR(S): Hummel, Gerd; Knolle, Jochen; Locardi, Elsa; Polakowski, Thomas; Scharn, Dirk; Schnatbaum, Karsten

PATENT ASSIGNEE(S): Jerini A.-G., Germany

SOURCE: Eur. Pat. Appl., 59 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1498422	A1	20050119	EP 2003-16233	20030717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004259282	A1	20050203	AU 2004-259282	20040719
CA 2532994	AA	20050203	CA 2004-2532994	20040719
WO 2005010030	A2	20050203	WO 2004-EP8057	20040719
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,				

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG

EP 1646643 A2 20060419 EP 2004-763337 20040719

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.:

EP 2003-16233

A 20030717

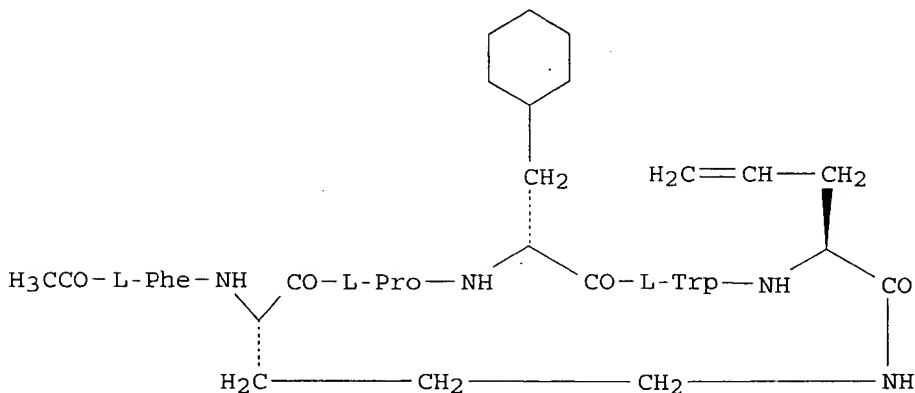
WO 2004-EP805.7

W 20040719

OTHER SOURCE(S): MARPAT 142:156325

ED Entered STN: 20 Jan 2005

GI



I

AB Title compds., e.g. (I), containing D- or unnatural amino acids, were prepared and tested for their activity as C5a receptor antagonists. Thus, I, similar cyclic compds., or non-cyclic free acids, amides, and/or N-terminal acylated derivs., were prepared by combined solid-phase and solution chemical (later steps of example preps. given). In in vitro enzyme release assay testing using rat blood cells carrying the C5a receptor, I had IC50 5 nM < I < 10 nM, with an EC50 value of » 1430 nM. Structure activity relationships of the claimed compds. was studied using a pharmacophore model of the compound's interaction with the receptor site. AB-permeability of two compds. (Ac-Phe[Orn-Pro-cha-Trp-Arg] and Ac-Phe[Orn-Hyp-cha-Trp-Phe]; cha - D-β-cyclohexylalanine) was studied using TC-7 cells.

IC ICM C07K007-06

ICS C07K014-47; C07K014-705; C07K007-50

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

ST oligopeptide analog prepn C5a receptor antagonist treatment disease; rheumatoid arthritis Lupus erythematosus psoriasis treatment C5a receptor antagonist; asthma septic shock multiple sclerosis treatment C5a receptor antagonist; pemphigus **inflammatory bowel** disease dermatomyositis treatment C5a receptor antagonist; lung disease myasthenia gravis treatment C5a receptor antagonist; cerebral apoplexy vasculitis reperfusion disorder treatment C5a receptor antagonist; central nervous system inflammation injury treatment C5a receptor antagonist

IT **Intestine, disease**

(inflammatory; Synthesis and evaluation of cyclic oligopeptide analogs as C5a receptor antagonists for treatment of **disease**)

IT 133254-16-7P 219639-70-0P 219639-75-5P 514814-62-1P 514814-76-7P  
514814-77-8P 514814-78-9P 827599-70-2P 827599-71-3P 827599-72-4P

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827599-84-8P	827599-85-9P	827599-86-0P	827599-87-1P	827599-88-2P
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RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Synthesis and evaluation of cyclic oligopeptide analogs as C5a receptor antagonists for treatment of disease).

IT 827600-12-4P

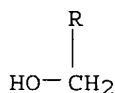
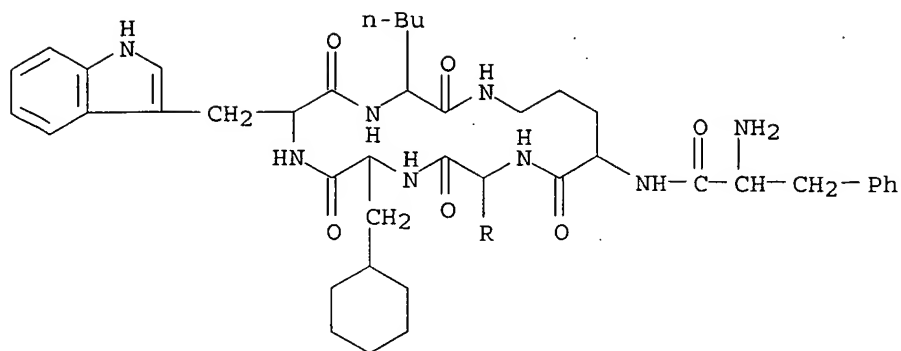
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Synthesis and evaluation of cyclic oligopeptide analogs as C5a receptor antagonists for treatment of disease)

RN 827600-12-4 CAPLUS

CN L-Norleucine, L-phenylalanyl-L-ornithyl-L-seryl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)





REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1036918 CAPLUS

DOCUMENT NUMBER: 142:765

TITLE: Method of treatment of systemic injury secondary to burns

INVENTOR(S): Shiels, Ian Alexander; Taylor, Steven Maxwell; Stocks, Shelli Z.

PATENT ASSIGNEE(S): The University of Queensland, Australia

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103392	A1	20041202	WO 2004-AU703	20040526
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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EP 1641482	A1	20060405	EP 2004-734788	20040526
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PRIORITY APPLN. INFO.:			AU 2003-902586	A 20030526
			WO 2004-AU703	W 20040526

OTHER SOURCE(S): MARPAT 142:765

ED Entered STN: 03 Dec 2004

AB The invention relates to the prevention or treatment of a systemic injury which is secondary to a burn, such as dysfunction or failure of an organ secondary to a burn, with an antagonist of a C5a receptor. In one embodiment the invention relates to the prevention or treatment of dysfunction or failure of the lung, kidney, bowel and/or liver which is secondary to a burn.

IC ICM A61K038-08

ICS A61K038-12; A61P017-02; A61P039-00; C07K007-56

CC 1-12 (Pharmacology)

IT Intestine, disease

Kidney, disease

Liver, disease

Lung, disease

Organ, animal, disease

(failure; treatment of systemic injury secondary to burns)

IT 219639-75-5, PMX 53 514814-34-7 514814-35-8 514814-36-9

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514814-67-6 514814-68-7 514814-69-8 514814-71-2 514814-72-3

514814-73-4 514814-74-5 514814-75-6 514814-76-7 514814-77-8

514814-78-9 514814-79-0 514814-80-3 514814-81-4 514814-83-6

514814-84-7 514814-85-8 514814-86-9 514814-87-0 514814-88-1

514814-89-2 514814-91-6 514814-92-7 514814-93-8 514814-94-9

514814-95-0 514814-96-1 514814-97-2 514814-98-3 615552-33-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(treatment of systemic injury secondary to burns)

IT 514814-52-9 514814-54-1

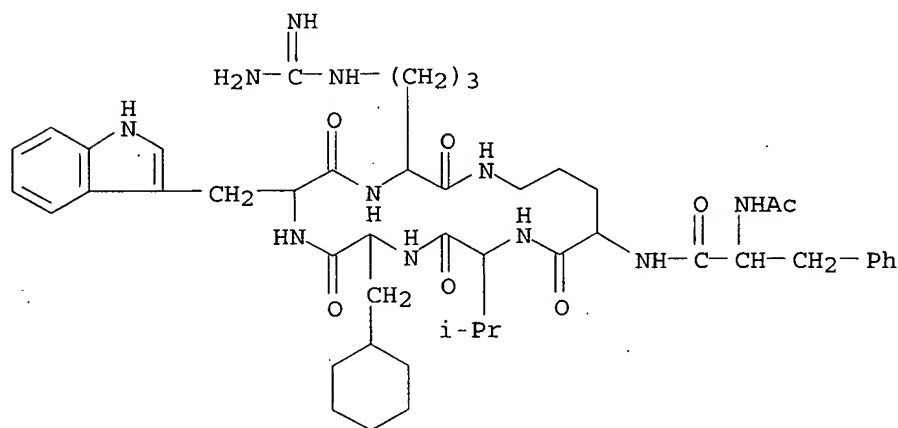
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(treatment of systemic injury secondary to burns)

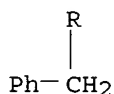
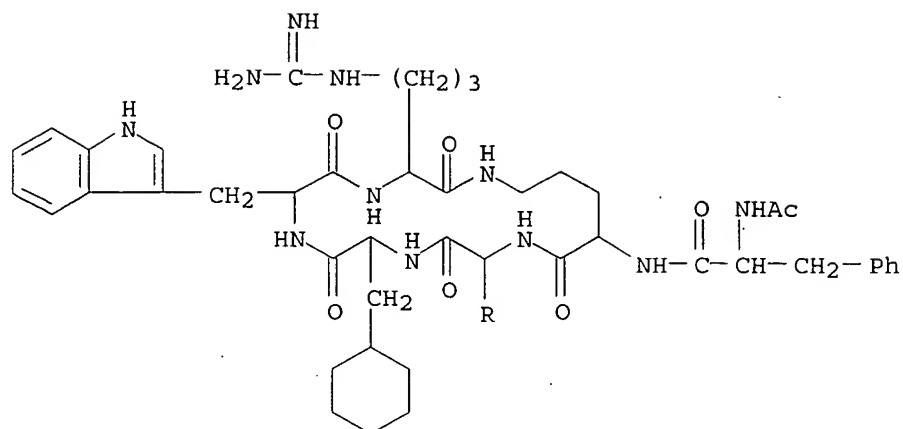
RN 514814-52-9 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-valyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)



RN 514814-54-1 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-phenylalanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:354812 CAPLUS

DOCUMENT NUMBER: 140:368676

TITLE: Treatment of hypersensitivity conditions with cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors

INVENTOR(S): Shiels, Ian Alexander; Taylor, Steven Maxwell; Fairlie, David

PATENT ASSIGNEE(S): The University of Queensland, Australia

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035080	A1	20040429	WO 2003-AU1374	20031016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003266862	A1	20040504	AU 2003-266862	20031016
EP 1560592	A1	20050810	EP 2003-747743	20031016

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2006505556 T2 20060216 JP 2004-543827 20031016  
PRIORITY APPLN. INFO.: AU 2002-952129 A 20021017  
WO 2003-AU1374 W 20031016

OTHER SOURCE(S): MARPAT 140:368676

ED Entered STN: 30 Apr 2004

AB This invention relates to methods of treatment of hypersensitivity conditions such as asthma and other allergic conditions, and especially to treatment of these conditions with cyclic peptidic and peptidomimetic compds. which have the ability to modulate the activity of G protein-coupled receptors. The compds. preferably act as antagonists of the C5a receptor, and are active against C5a receptors on polymorphonuclear leukocytes and macrophages. Particularly preferred compds. for use in the methods of the invention are disclosed. Dogs with allergic dermatitis were treated with cyclic peptide PMX53 (AcF-[OPdChaWR]).

IC ICM A61K038-08

ICS A61K038-12; A61P011-06; A61P037-08

CC 1-7 (Pharmacology)

Section cross-reference(s): 15, 34

ST cyclic peptide inhibitor **G protein** coupled receptor hypersensitivity; peptidomimetic inhibitor **G protein** coupled receptor hypersensitivity; C5a receptor antagonist treatment hypersensitivity; allergic dermatitis dog treatment cyclic peptide PMX53

IT Immunity

(Arthus phenomenon, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)

IT Complement receptors

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(C5a, inhibitors; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)

IT Allergy

(allergic dermatitis, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)

IT Dermatitis

(allergic, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)

IT Siphonaptera

(allergy to, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)

IT Dermatitis

(atopic, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)

IT Allergy inhibitors

Anti-inflammatory agents

Antiasthmatics

Human

Peptidomimetics

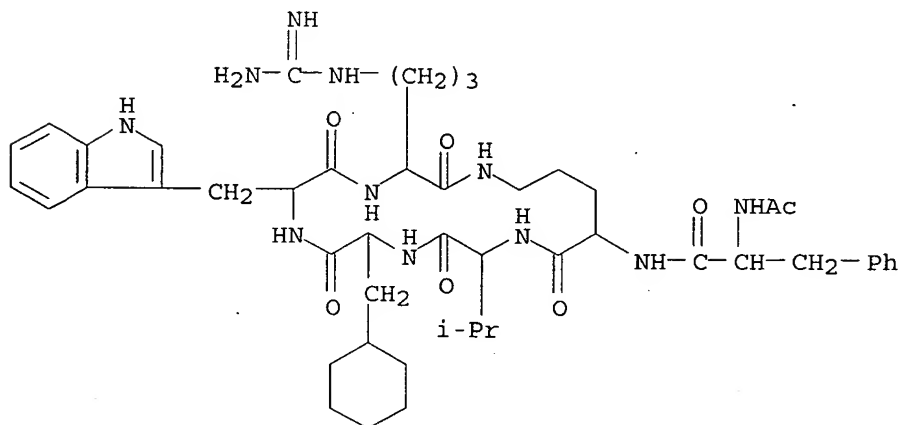
Physiological saline solutions

(cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)

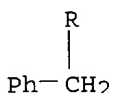
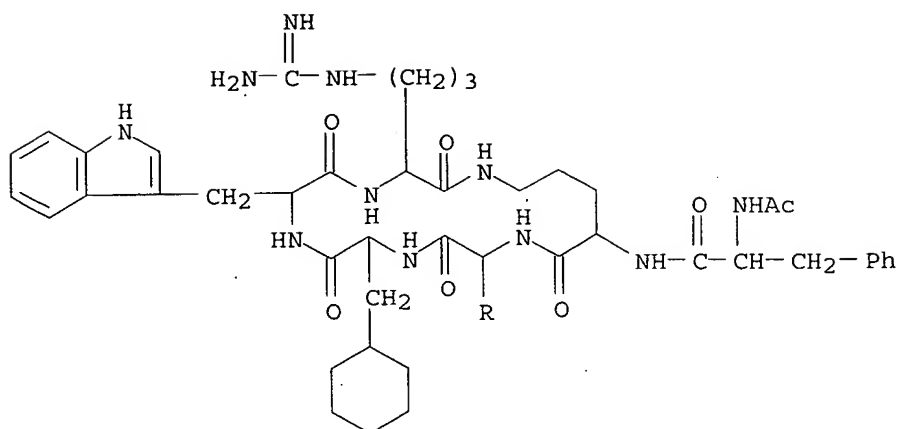
- IT Interleukin 6  
Tumor necrosis factors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Polyoxyalkylenes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Peptides, biological studies  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Eosinophil  
(disease, hypereosinophilic syndrome, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Lung, disease  
(farmer's lung, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Inflammation  
Kidney, disease  
(glomerulonephritis, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Blood, disease  
(hypereosinophilic syndrome, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Allergy  
(hypersensitivity, treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Allergy  
(immediate hypersensitivity, type II (cytotoxic) or type III (complex-mediated), treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Intestine, disease  
(inflammatory, inhibitor used in conjunction with other agents for treatment of; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Drug delivery systems  
(inhalants; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT Macrophage  
Polymorphonuclear leukocyte  
(inhibition of C5a receptor on; cyclic peptide and peptidomimetic inhibitors of **G protein**-coupled receptors for treatment of hypersensitivity conditions)
- IT **G protein**-coupled receptors  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

- (inhibitors; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Drug delivery systems  
(injections, s.c.; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Skin, disease  
(mange, demodectic, treatment of; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Drug delivery systems  
(nasal; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Drug delivery systems  
(oral; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Drug delivery systems  
(topical; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Canis familiaris  
(treatment of allergic dermatitis in; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Felis catus  
Panthera tigris tigris  
(treatment of asthma in; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Demodex canis  
(treatment of dermatitis from; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT Allergy  
Asthma  
Dermatitis  
Eczema  
(treatment of; cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)
- IT 219639-75-5, PMX 53 514814-34-7 514814-35-8 514814-36-9  
514814-37-0 514814-38-1 514814-42-7 514814-43-8 514814-44-9  
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514814-95-0 514814-96-1 514814-97-2 514814-98-3 514814-99-4  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(cyclic peptide and peptidomimetic inhibitors of G protein-coupled receptors for treatment of hypersensitivity conditions)

- IT 64-17-5, Ethanol, biological studies 67-68-5, DMSO, biological studies  
7732-18-5, Water, biological studies 25322-68-3  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic peptide and peptidomimetic inhibitors of G  
protein-coupled receptors for treatment of hypersensitivity  
conditions)
- IT 170277-31-3, Infliximab  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitor used in conjunction with; cyclic peptide and peptidomimetic  
inhibitors of G protein-coupled receptors for  
treatment of hypersensitivity conditions)
- IT 80295-42-7, C3a  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors, inhibitor used in conjunction with; cyclic peptide and  
peptidomimetic inhibitors of G protein-coupled  
receptors for treatment of hypersensitivity conditions)
- IT 514815-00-0  
RL: PRP (Properties)  
(unclaimed; treatment of hypersensitivity conditions with cyclic  
peptide and peptidomimetic inhibitors of G protein  
-coupled receptors)
- IT 514814-52-9 514814-54-1  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(cyclic peptide and peptidomimetic inhibitors of G  
protein-coupled receptors for treatment of hypersensitivity  
conditions)
- RN 514814-52-9 CAPLUS  
CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-valyl-3-cyclohexyl-D-  
alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



- RN 514814-54-1 CAPLUS  
CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-phenylalanyl-3-cyclohexyl-  
D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:354811 CAPLUS

DOCUMENT NUMBER: 140:368675

TITLE: **G protein-coupled**  
receptor-modulating cyclic peptides and peptidomimetic  
compounds for the treatment of osteoarthritis  
Shiels, Ian Alexander; Taylor, Steven Maxwell  
INVENTOR(S):  
PATENT ASSIGNEE(S): The University of Queensland, Australia  
SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035079	A1	20040429	WO 2003-AU1373	20031016
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003269609	A1	20040504	AU 2003-269609	20031016
EP 1575606	A1	20050921	EP 2003-750172	20031016
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			



JP 2006505555 T2 20060216 JP 2004-543826 20031016  
 PRIORITY APPLN. INFO.: AU 2002-952086 A 20021016  
 WO 2003-AU1373 W 20031016

OTHER SOURCE(S): MARPAT 140:368675

ED Entered STN: 30 Apr 2004

AB The invention discloses methods for treatment of osteoarthritis, and especially to treatment of this condition with cyclic peptidic and peptidomimetic compds. which have the ability to modulate the activity of G protein-coupled receptors. The compds. preferably act as antagonists of the C5a receptor, and are active against C5a receptors on polymorphonuclear leukocytes and macrophages.

IC ICM A61K038-08

ICS A61K038-12; A61P019-02

CC 1-7 (Pharmacology)

ST G protein coupled receptor modulator cyclic peptide peptidomimetic osteoarthritis

IT Complement receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (C5a; G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis).

IT Antiarthritics

Osteoarthritis

Peptidomimetics

(G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

IT G protein-coupled receptors

Interleukin 6

RL: BSU (Biological study, unclassified); BIOL (Biological study) (G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

IT Tumor necrosis factors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (TNF- $\alpha$ ; G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

IT Peptides, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cyclic; G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

IT Immunity

(reverse passive Arthus phenomenon; G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

IT 80295-54-1, Complement C5a

RL: BSU (Biological study, unclassified); BIOL (Biological study) (G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

IT 219639-70-0 219639-75-5 514814-34-7 514814-35-8 514814-36-9  
 514814-37-0 514814-38-1 514814-42-7 514814-43-8 514814-44-9  
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 514814-88-1 514814-89-2 514814-91-6 514814-92-7 514814-93-8  
 514814-94-9 514814-99-4 615552-33-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

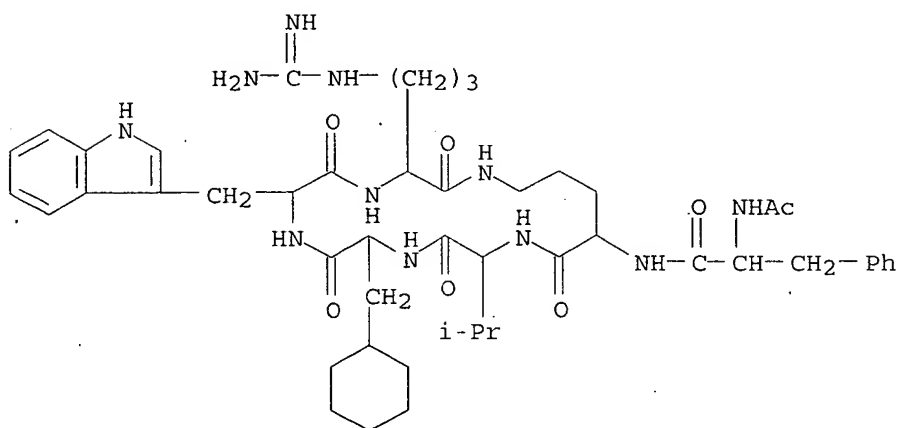
IT 514814-52-9 514814-54-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of osteoarthritis)

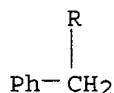
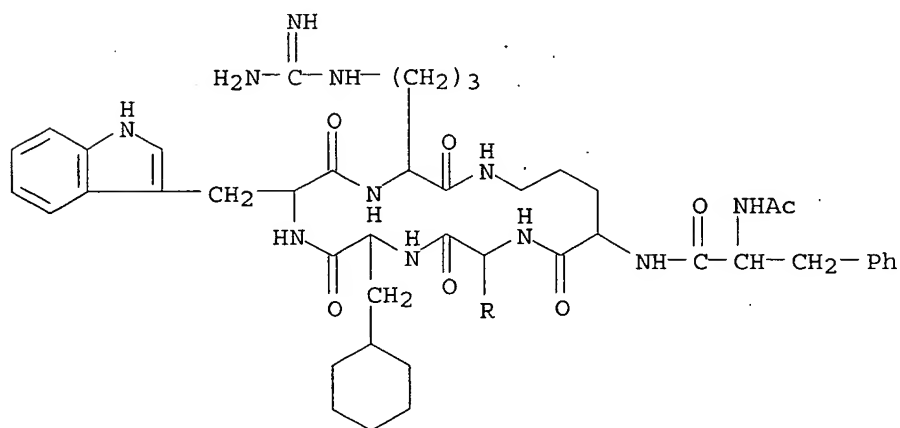
RN 514814-52-9 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-valyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



RN 514814-54-1 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-phenylalanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:354810 CAPLUS  
 DOCUMENT NUMBER: 140:332495  
 TITLE: **G protein-coupled**  
 receptor-modulating cyclic peptides and peptidomimetic  
 compounds for the treatment of **inflammatory**  
**bowel disease**  
 INVENTOR(S): Woodruff, Trent Martin; Taylor, Steven  
 PATENT ASSIGNEE(S): The University of Queensland, Australia  
 SOURCE: PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035078	A1	20040429	WO 2003-AU1365	20031015
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003269602	A1	20040504	AU 2003-269602	20031015
EP 1558277	A1	20050803	EP 2003-750165	20031015
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006505621	T2	20060216	JP 2005-501247	20031015
PRIORITY APPLN. INFO.:			AU 2002-952084	A 20021016
			AU 2003-902452	A 20030520
			WO 2003-AU1365	W 20031015

OTHER SOURCE(S): MARPAT 140:332495

ED Entered STN: 30 Apr 2004

AB The invention discloses methods for treatment of inflammatory bowel disease, and especially to treatment of this condition with cyclic peptidic and peptidomimetic compds. which have the ability to modulate the activity of G protein-coupled receptors. The compds. preferably act as antagonists of the C5a receptor, and are active against C5a receptors on polymorphonuclear leukocytes and macrophages.

IC ICM A61K038-08

ICS A61K038-12; A61P029-00; A61P001-00

CC 1-7 (Pharmacology)

ST **G protein coupled receptor modulator**

**inflammatory bowel disease treatment; cyclic peptide**  
**peptidomimetic inflammatory bowel disease treatment**

IT Complement receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (C5a; **G protein-coupled receptor-modulating cyclic**  
**peptides and peptidomimetics for treatment of inflammatory**  
**bowel disease)**

IT Inflammation

(**Crohn's disease; G protein-coupled**  
**receptor-modulating cyclic peptides and peptidomimetics for treatment**  
**of inflammatory bowel disease)**

IT Intestine, disease

- (Crohn's; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)
- IT Anti-inflammatory agents
  - Celiac disease
  - Gastrointestinal agents
  - Human
  - Peptidomimetics
    - (G protein-coupled receptor-modulating cyclic  
peptides and peptidomimetics for treatment of inflammatory  
bowel disease)
- IT G protein-coupled receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (G protein-coupled receptor-modulating cyclic  
peptides and peptidomimetics for treatment of inflammatory  
bowel disease)
- IT Tumor necrosis factors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (TNF- $\alpha$ ; G protein-coupled receptor-modulating  
cyclic peptides and peptidomimetics for treatment of  
inflammatory bowel disease)
- IT Canis familiaris
  - (canine lymphocytic-plasmocytic colitis; G  
protein-coupled receptor-modulating cyclic peptides and  
peptidomimetics for treatment of inflammatory bowel  
disease)
- IT Drug delivery systems
  - (capsules, enteric-coated; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)
- IT Inflammation
  - Intestine, disease
    - (colitis, canine lymphocytic-plasmocytic; G  
protein-coupled receptor-modulating cyclic peptides and  
peptidomimetics for treatment of inflammatory bowel  
disease)
- IT Inflammation
  - Intestine, disease
    - (colitis, collagenous; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)
- IT Inflammation
  - Intestine, disease
    - (colitis, infectious; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)
- IT Inflammation
  - Intestine, disease
    - (colitis, lymphocytic; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)
- IT Inflammation
  - Intestine, disease
    - (colitis, protothecal; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)
- IT Inflammation
  - Intestine, disease
    - (colitis, pseudomembranous; G protein  
-coupled receptor-modulating cyclic peptides and peptidomimetics for

treatment of inflammatory bowel disease)

IT Inflammation  
Intestine, disease  
(colitis; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)

IT Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(cyclic; G protein-coupled receptor-modulating  
cyclic peptides and peptidomimetics for treatment of  
inflammatory bowel disease)

IT Inflammation  
Intestine, disease  
(enteritis, lymphocytic-plasmocytic; G  
protein-coupled receptor-modulating cyclic peptides and  
peptidomimetics for treatment of inflammatory bowel  
disease)

IT Inflammation  
Intestine, disease  
(enterocolitis, eosinophilic; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)

IT Inflammation  
Intestine, disease  
(enterocolitis; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)

IT Intestine, disease  
(inflammatory, ischemic; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)

IT Intestine, disease  
(inflammatory; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)

IT Drug delivery systems  
(rectal; G protein-coupled receptor-modulating  
cyclic peptides and peptidomimetics for treatment of  
inflammatory bowel disease)

IT Inflammation  
Intestine, disease  
(ulcerative colitis, histocytic; G protein  
-coupled receptor-modulating cyclic peptides and peptidomimetics for  
treatment of inflammatory bowel disease)

IT Inflammation  
Intestine, disease  
(ulcerative colitis; G protein-coupled  
receptor-modulating cyclic peptides and peptidomimetics for treatment  
of inflammatory bowel disease)

IT 514814-34-7 514814-35-8 514814-36-9 514814-37-0 514814-38-1  
514814-42-7 514814-43-8 514814-44-9 514814-45-0 514814-46-1  
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514814-54-1 514814-57-4 514814-58-5 514814-60-9  
514814-62-1 514814-63-2 514814-65-4 514814-66-5 514814-67-6  
514814-68-7 514814-69-8 514814-71-2 514814-72-3 514814-73-4  
514814-74-5 514814-75-6 514814-76-7 514814-77-8 514814-78-9  
514814-79-0 514814-80-3 514814-81-4 514814-83-6 514814-84-7  
514814-85-8 514814-86-9 514814-87-0 514814-88-1 514814-89-2  
514814-91-6 514814-92-7 514814-93-8 514814-94-9 514814-95-0

514814-96-1 514814-97-2 514814-98-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(G protein-coupled receptor-modulating cyclic peptides and peptidomimetics)

IT 80295-42-7, Complement C3a 80295-54-1, Complement C5a

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of inflammatory bowel disease)

IT 50-24-8, Prednisolone 170277-31-3, Infliximab 219639-75-5, PMX 53

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(G protein-coupled receptor-modulating cyclic peptides and peptidomimetics for treatment of inflammatory bowel disease)

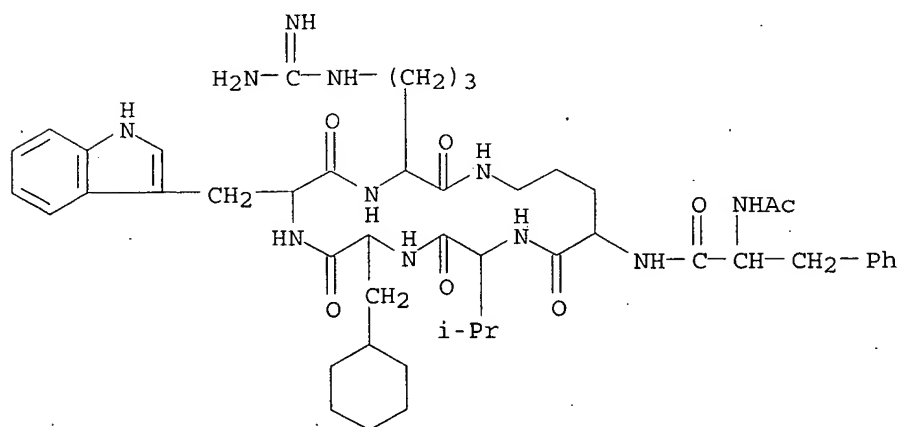
IT 514814-52-9 514814-54-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(G protein-coupled receptor-modulating cyclic peptides and peptidomimetics)

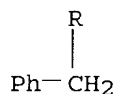
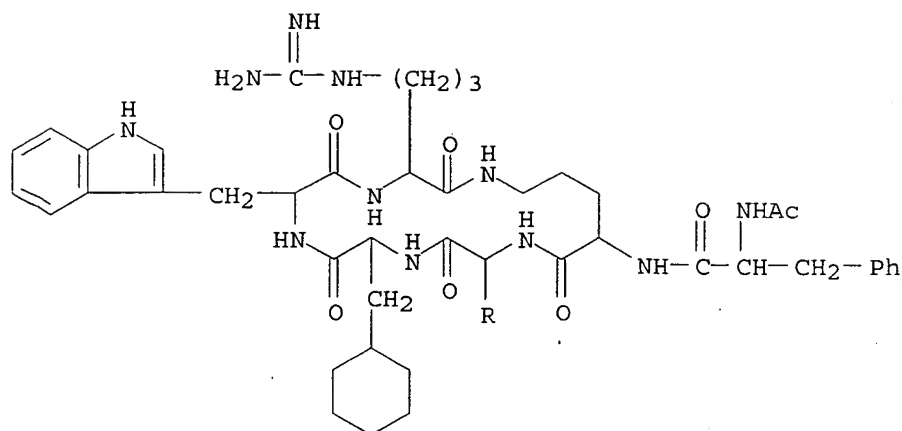
RN 514814-52-9 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-valyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



RN 514814-54-1 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-phenylalanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:836884 CAPLUS

DOCUMENT NUMBER: 139:333147

TITLE: Use of C5a receptor antagonist in the treatment of fibrosis

INVENTOR(S): Taylor, Stephen Maxwell; Shiels, Ian Alexander; Brown, Lindsay Charles

PATENT ASSIGNEE(S): Promics Pty Limited, Australia

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086448	A1	20031023	WO 2003-AU415	20030407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003215446	A1	20031027	AU 2003-215446	20030407
EP 1496929	A1	20050119	EP 2003-746152	20030407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

JP 2005529872 T2 20051006 JP 2003-583466 20030407  
 PRIORITY APPLN. INFO.: AU 2002-1606 A 20020408  
 WO 2003-AU415 W 20030407

OTHER SOURCE(S): MARPAT 139:333147

ED Entered STN: 24 Oct 2003

AB The invention discloses the use of an antagonist of a G protein-coupled receptor in the prevention and/or treatment of fibrosis, e.g. the treatment of fibrosis associated with myocardial infarction or diabetes or certain pulmonary conditions. In a preferred embodiment, the antagonist is a C5a receptor antagonist, more preferably a cyclic peptide antagonist of the C5a receptor. In particular, the invention provides a method of prevention, treatment or alleviation of a fibrotic condition, comprising the step of administering an effective amount of an antagonist of a G protein-coupled receptor to a subject in need of such treatment.

IC ICM A61K038-04

ICS A61K039-395; A61K038-08; A61P013-12; A61P009-10; A61P011-00

CC 1-12 (Pharmacology)

ST G protein coupled receptor antagonist fibrosis treatment; C5a receptor antagonist fibrosis treatment

IT G protein-coupled receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; C5a receptor antagonist in treatment of fibrosis)

IT 219639-75-5, PMX 53 514814-34-7 514814-35-8 514814-36-9  
 514814-37-0 514814-38-1 514814-42-7 514814-43-8 514814-44-9  
 514814-45-0 514814-46-1 514814-47-2 514814-49-4 514814-52-9  
 514814-54-1 514814-57-4 514814-58-5 514814-60-9  
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 514814-74-5 514814-75-6 514814-76-7 514814-77-8 514814-78-9  
 514814-79-0 514814-80-3 514814-81-4 514814-83-6 514814-84-7  
 514814-85-8 514814-86-9 514814-87-0 514814-88-1 514814-89-2  
 514814-91-6 514814-92-7 514814-93-8 514814-94-9 514814-97-2  
 514814-98-3 615552-30-2 615552-33-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (C5a receptor antagonist in treatment of fibrosis)

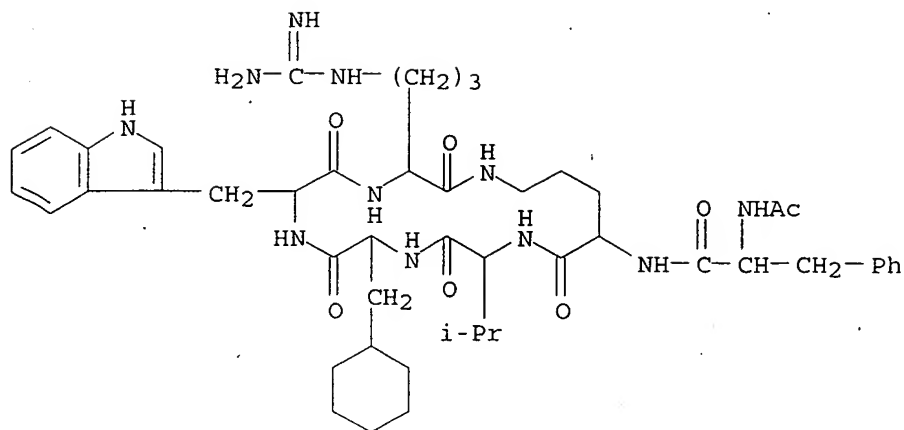
IT 514814-52-9 514814-54-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (C5a receptor antagonist in treatment of fibrosis)

RN 514814-52-9 CAPLUS

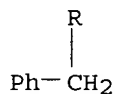
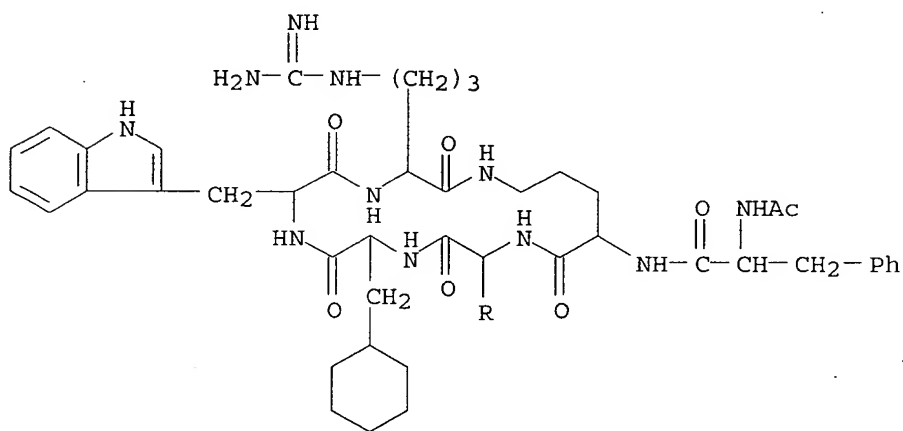
CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-valyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)





RN 514814-54-1 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-phenylalanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:319928 CAPLUS

DOCUMENT NUMBER: 138:331692

TITLE: Cyclic peptides and peptidomimetic compounds as G protein-coupled receptor antagonists, and therapeutic use

INVENTOR(S): Taylor, Steve; Shields, Ian Alexander

PATENT ASSIGNEE(S): University of Queensland, Australia

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033528	A1	20030424	WO 2002-AU1427	20021017
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2463675	AA	20030424	CA 2002-2463675	20021017
EP 1444251	A1	20040811	EP 2002-771873	20021017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1604909	A	20050406	CN 2002-825257	20021017
JP 2005515973	T2	20050602	JP 2003-536266	20021017
PRIORITY APPLN. INFO.:			AU 2001-8334	A 20011017
			WO 2002-AU1427	W 20021017

OTHER SOURCE(S): MARPAT 138:331692

ED Entered STN: 25 Apr 2003

AB The invention provides cyclic compds. which have the ability to modulate the activity of G protein-coupled receptors. The compds. preferably act as antagonists. In preferred embodiments, the invention provides cyclic peptidic and peptidomimetic antagonists of C5a receptors, which are active against C5a receptors on polymorphonuclear leukocytes and macrophages. The compds. of the invention are both potent and selective, and are useful in the treatment of a variety of inflammatory conditions.

IC ICM C07K007-56

ICS A61K038-08; A61P011-00; A61P009-10; A61P017-00; A61P037-00

CC 1-7 (Pharmacology)

Section cross-reference(s): 34

ST **G protein** coupled receptor antagonist cyclic peptidomimetic peptide prepn; antiinflammatory **G protein** coupled receptor antagonist cyclic peptidomimetic peptide; c5a receptor antagonist cyclic peptidomimetic peptide

IT Immunity

(Arthus phenomenon; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

IT Complement receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (C5a; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

IT Tumor necrosis factors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (TNF- $\alpha$ ; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

IT Respiratory distress syndrome

(adult; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

IT Antiarteriosclerotics

(antiatherosclerotics; cyclic peptides and peptidomimetic compds. as

- G protein-coupled receptor antagonists, and therapeutic use)**
- IT Ischemia  
(cardiac; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Dermatitis  
(contact; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Alzheimer's disease  
Anti-Alzheimer's agents  
Anti-inflammatory agents  
Anti-ischemic agents  
Antiarthritics  
Antiasthmatics  
Antirheumatic agents  
Asthma  
Atherosclerosis  
Cardiovascular agents  
Central nervous system, disease  
Dermatitis  
Drug delivery systems  
Eczema  
Fibrosis  
Multiple sclerosis  
Nervous system agents  
Neutrophil  
Peptidomimetics  
Pharmacophores  
Polymorphonuclear leukocyte  
Psoriasis  
Rheumatoid arthritis  
Transplant rejection  
(cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT **G protein-coupled receptors**  
Haptoglobin  
Interleukin 6  
Tachykinin receptors  
Vasopressin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Mental and behavioral disorders  
(dementia; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Muscle  
(edema; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Disease, animal  
(extracorporeal post-dialysis syndrome; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Gingiva, disease  
Inflammation  
(gingivitis; cyclic peptides and peptidomimetic compds. as **G**

**protein-coupled receptor antagonists, and therapeutic use)**

IT Lung, disease  
 Reperfusion  
 (injury; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Ischemia  
 (intestinal; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Heart, disease  
**Intestine, disease**  
 (ischemia; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Ischemia  
 (limb; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Arthritis  
 (monoarticular; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Agranulocytosis  
 (neutropenia; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Proteins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (proteinuria; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Injury  
 (pulmonary; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Injury  
 (reperfusion; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Shock (circulatory collapse)  
 (septic; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Lupus erythematosus  
 (systemic; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Drug delivery systems  
 (topical; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT 57-13-6, Urea, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (blood urea nitrogen; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT 60-27-5, Creatinine 7440-09-7, Potassium, biological studies  
 7440-70-2, Calcium, biological studies 9000-86-6, Alanine transaminase  
 9000-97-9, Aspartate aminotransferase 9001-15-4, Creatine kinase  
 9001-60-9, Lactate dehydrogenase 9003-99-0, Myeloperoxidase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT 219639-75-5P 514814-34-7P 514814-35-8P 514814-36-9P 514814-37-0P  
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 514814-81-4P 514814-83-6P 514814-84-7P 514814-85-8P 514814-86-9P

- G protein-coupled receptor antagonists, and therapeutic use)**
- IT Ischemia
  - (cardiac; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Dermatitis
  - (contact; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Alzheimer's disease
  - Anti-Alzheimer's agents
  - Anti-inflammatory agents
  - Anti-ischemic agents
  - Antiarthritics
  - Antiasthmatics
  - Antirheumatic agents
  - Asthma
  - Atherosclerosis
  - Cardiovascular agents
  - Central nervous system, disease
  - Dermatitis
  - Drug delivery systems
  - Eczema
  - Fibrosis
  - Multiple sclerosis
  - Nervous system agents
  - Neutrophil
  - Peptidomimetics
  - Pharmacophores
  - Polymorphonuclear leukocyte
  - Psoriasis
  - Rheumatoid arthritis
  - Transplant rejection
    - (cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT **G protein-coupled receptors**
  - Haptoglobin
  - Interleukin 6
  - Tachykinin receptors
  - Vasopressin receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Peptides, biological studies
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (cyclic; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Mental and behavioral disorders
  - (dementia; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Muscle
  - (edema; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Disease, animal
  - (extracorporeal post-dialysis syndrome; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**
- IT Gingiva, disease
  - Inflammation
    - (gingivitis; cyclic peptides and peptidomimetic compds. as **G**

**protein-coupled receptor antagonists, and therapeutic use)**

IT Lung, disease  
Reperfusion  
(injury; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Ischemia  
(intestinal; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Heart, disease  
**Intestine, disease**  
(ischemia; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Ischemia  
(limb; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Arthritis  
(monoarticular; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Agranulocytosis  
(neutropenia; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(proteinuria; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Injury  
(pulmonary; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Injury  
(reperfusion; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Shock (circulatory collapse)  
(septic; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Lupus erythematosus  
(systemic; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT Drug delivery systems  
(topical; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT 57-13-6, Urea, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood urea nitrogen; cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT 60-27-5, Creatinine 7440-09-7, Potassium, biological studies  
7440-70-2, Calcium, biological studies 9000-86-6, Alanine transaminase  
9000-97-9, Aspartate aminotransferase 9001-15-4, Creatine kinase  
9001-60-9, Lactate dehydrogenase 9003-99-0, Myeloperoxidase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cyclic peptides and peptidomimetic compds. as **G protein-coupled receptor antagonists, and therapeutic use)**

IT 219639-75-5P 514814-34-7P 514814-35-8P 514814-36-9P 514814-37-0P  
514814-38-1P 514814-42-7P 514814-43-8P 514814-44-9P 514814-45-0P  
514814-46-1P 514814-47-2P 514814-49-4P 514814-51-8P  
514814-52-9P 514814-54-1P 514814-57-4P 514814-58-5P  
514814-60-9P 514814-62-1P 514814-63-2P 514814-65-4P 514814-66-5P  
514814-67-6P 514814-68-7P 514814-71-2P 514814-72-3P 514814-73-4P  
514814-74-5P 514814-75-6P 514814-76-7P 514814-77-8P 514814-80-3P  
514814-81-4P 514814-83-6P 514814-84-7P 514814-85-8P 514814-86-9P

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033528	A1	20030424	WO 2002-AU1427	20021017
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2463675	AA	20030424	CA 2002-2463675	20021017
EP 1444251	A1	20040811	EP 2002-771873	20021017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1604909	A	20050406	CN 2002-825257	20021017
JP 2005515973	T2	20050602	JP 2003-536266	20021017
PRIORITY APPLN. INFO.:			AU 2001-8334	A 20011017
			WO 2002-AU1427	W 20021017

OTHER SOURCE(S): MARPAT 138:331692

ED Entered STN: 25 Apr 2003

AB The invention provides cyclic compds. which have the ability to modulate the activity of G-protein-coupled receptors. The compds. preferably act as antagonists. In preferred embodiments, the invention provides cyclic peptidic and peptidomimetic antagonists of C5a receptors, which are active against C5a receptors on polymorphonuclear leukocytes and macrophages. The compds. of the invention are both potent and selective, and are useful in the treatment of a variety of inflammatory conditions.

IC ICM C07K007-56

ICS A61K038-08; A61P011-00; A61P009-10; A61P017-00; A61P037-00

CC 1-7 (Pharmacology)

Section cross-reference(s): 34

ST **G protein** coupled receptor antagonist cyclic peptidomimetic peptide prepn; antiinflammatory **G protein** coupled receptor antagonist cyclic peptidomimetic peptide; c5a receptor antagonist cyclic peptidomimetic peptide

IT Immunity

(Arthus phenomenon; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

IT Complement receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (C5a; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

IT Tumor necrosis factors

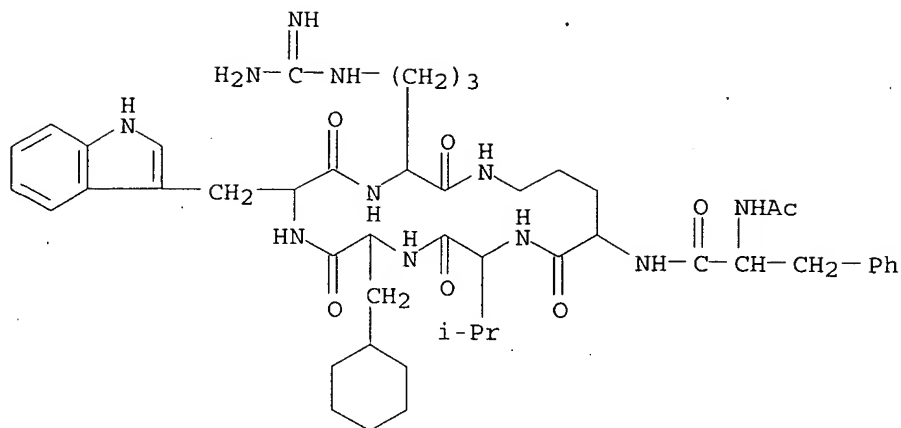
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TNF- $\alpha$ ; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

IT Respiratory distress syndrome

(adult; cyclic peptides and peptidomimetic compds. as **G protein**-coupled receptor antagonists, and therapeutic use)

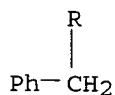
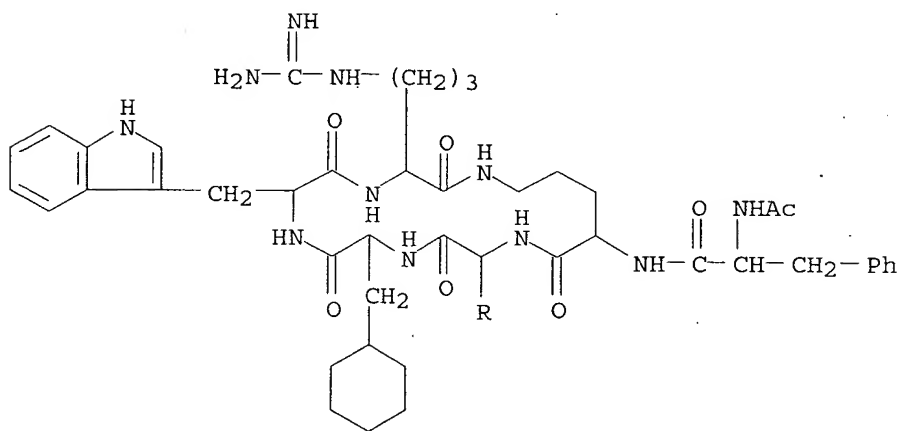
IT Antiarteriosclerotics

(antiatherosclerotics; cyclic peptides and peptidomimetic compds. as



RN 514814-54-1 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-phenylalanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:319928 CAPLUS

DOCUMENT NUMBER: 138:331692

TITLE: Cyclic peptides and peptidomimetic compounds as G protein-coupled receptor antagonists, and therapeutic use

INVENTOR(S): Taylor, Steve; Shields, Ian Alexander

PATENT ASSIGNEE(S): University of Queensland, Australia

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2



PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008189	A1	20020131	WO 2001-AU898	20010724
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2417127	AA	20020131	CA 2001-2417127	20010724
EP 1309552	A1	20030514	EP 2001-951251	20010724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004503604	T2	20040205	JP 2002-514096	20010724
US 2004033995	A1	20040219	US 2003-333871	20030825
PRIORITY APPLN. INFO.:			AU 2000-8965	A 20000724
			AU 2000-1669	A 20001124
			WO 2001-AU898	W 20010724

OTHER SOURCE(S): MARPAT 136:134497

AB Title compds. I [X = CRR'CO<sub>2</sub>H, CRR'-tetrazolyl, CRR'SO<sub>3</sub>H, CRR'P(O)(OH)<sub>2</sub>, CRR'P(O)(OH)(OR"), CHRCH<sub>2</sub>CO<sub>2</sub>H, CHRCH<sub>2</sub>-tetrazolyl, CHRCH<sub>2</sub>SO<sub>3</sub>H, CHRCH<sub>2</sub>P(O)(OH)<sub>2</sub>, CHRCH<sub>2</sub>P(O)(OH)(OR"), OP(O)(OH)R', NRSO<sub>3</sub>H, NRP(O)(OH)<sub>2</sub>, NRP(O)(OH)(OR''); R, R', R'' = H, (un)substituted alk(en/yn)yl, acyl, arylalkyl, cycloalkylalkyl, heterocyclalkyl, except that R'' is not hydrogen; Q = acyl, carboxamido, sulfonyl, sulfinyl, phosphinyl, etc.] were prepared For example, II was synthesized from N-Boc-D-histidine in 11 steps. II had IC<sub>50</sub> = 2.5 μM for human non-pancreatic secretory phospholipase A<sub>2</sub> (sPLA<sub>2</sub>). Homochiral and enantiomeric mixts. of I are useful for treatment of (e.g.) inflammatory diseases.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt;

ACCESSION NUMBER: 2003:758632 CAPLUS  
DOCUMENT NUMBER: 139:391088  
TITLE: Comparative protection against rat intestinal  
reperfusion injury by a new inhibitor of sPLA2, COX-1  
and COX-2 selective inhibitors, and an LTC4 receptor  
antagonist  
AUTHOR(S): Arumugam, Thiruma V.; Arnold, Naomi; Proctor, Lavinia  
M.; Newman, Michelle; Reid, Robert C.; Hansford, Karl  
A.; Fairlie, David P.; Shiels, Ian A.;  
Taylor, Stephen M.  
CORPORATE SOURCE: Department of Physiology and Pharmacology, School of  
Biomedical Sciences, University of Queensland, St.  
Lucia, 4072, Australia  
SOURCE: British Journal of Pharmacology (2003), 140(1), 71-80  
CODEN: BJPCBM; ISSN: 0007-1188  
PUBLISHER: Nature Publishing Group  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A new group IIa sPLA2 inhibitor was compared with selective inhibitors of  
COX-1, COX-2 and an LTC4 antagonist for effects on local and remote tissue  
injuries following ischemia and reperfusion (I/R) of the small intestine  
in rats. In an acute model of ischemia (30 min) and reperfusion (150 min)  
injury in the absence of inhibitors, there was significant intestinal  
hemorrhage, edema and mucosal damage, neutropenia, elevated serum levels  
of aspartate aminotransferase (AST) and hypotension. Preischemic  
treatment with the inhibitor of sPLA2 (Group IIa), at 5 mg kg<sup>-1</sup> i.v. or 10  
mg kg<sup>-1</sup> p.o. significantly inhibited I/R-induced neutropenia, the  
elevation of serum levels of AST, intestinal edema and hypotension.  
Pretreatment with the COX-2 inhibitor celebrex (10 mg kg<sup>-1</sup> i.v.) and the  
LTC4 antagonist zafirlukast (1 mg kg<sup>-1</sup> i.v.) also showed marked  
improvement with I/R-induced AST, edema and neutropenia. Hypotension was  
only reduced by the LTC4 antagonist. The COX-1 inhibitor flunixin (1 mg  
kg<sup>-1</sup> i.v.) did not effect improvement in the markers of tissue injury.  
Histol. examination of rat I/R injury showed that all of the drugs offered some  
protection to the mucosal layer damage compared to no drug treatment.  
Given i.v., the sPLA2 inhibitor was more effective than either the COX-1  
or COX-2 inhibitors in preventing rat I/R injury. These results indicate  
that a potent new inhibitor of sPLA2 (group IIa) protects the rat small  
intestine from I/R injury after oral or i.v. administration. COX-2 and  
LTC4 inhibitors also showed some beneficial effects against intestinal I/R  
injury. Our study suggests that sPLA2 (Group IIa) may have a pathogenic  
role in intestinal I/R in rats.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:90009 CAPLUS  
DOCUMENT NUMBER: 136:134497  
TITLE: Synthesis and use of amino acid-derived aliphatic  
amides/esters as inhibitors of phospholipases  
INVENTOR(S): Reid, Robert C.; Clark, Christopher I.; Hansford,  
Karl; Stoermer, Martin J.; McGeary, Ross P.;  
Fairlie, David P.  
PATENT ASSIGNEE(S): The University of Queensland, Australia  
SOURCE: PCT Int. Appl., 109 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

antagonists supports the importance of a turn for receptor binding. Competition between a cyclic antagonist and either C5a or an acyclic agonist for C5aR on PMNLs supports a common or overlapping binding site on the C5aR. Structure-activity relationships for 60 cyclic analogs were evaluated by competitive radioligand binding with C5a (affinity) and myeloperoxidase release (antagonist potency) from human PMNLs, with 20 compds. having high antagonist potencies (IC<sub>50</sub>, 20 nM - 1  $\mu$ M). Computer modeling comparisons reveal that potent antagonists share a common cyclic backbone shape, with affinity-determining side chains of defined volume projecting from the cyclic scaffold. These results define a new pharmacophore for C5a antagonist development and advance our understanding of ligand recognition and receptor activation of this G protein-coupled receptor.

REFERENCE COUNT: 41. THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:878195 CAPLUS

DOCUMENT NUMBER: 140:104944

TITLE: A Potent Human C5a Receptor Antagonist Protects against Disease Pathology in a Rat Model of Inflammatory Bowel Disease

AUTHOR(S): Woodruff, Trent M.; Arumugam, Thiruma V.; Shiels, Ian A.; Reid, Robert C.; Fairlie, David P.; Taylor, Stephen M.

CORPORATE SOURCE: School of Biomedical Sciences, Department of Physiology and Pharmacology, University of Queensland, Brisbane, QLD 4072, Australia

SOURCE: Journal of Immunology (2003), 171(10), 5514-5520  
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The complement system is implicated in the pathogenesis of human inflammatory bowel disease, but the specific role of C5a has never been examined. We have compared the efficacy of an orally active human C5a receptor antagonist (AcPhe[Orn-Pro-D-cyclohexylalanine-Trp-Arg]), prednisolone, and infliximab against trinitrobenzene sulfonic acid (TNBS)-induced colitis in rats. The drugs were administered either 2 days before or 24 h after TNBS instillation, and rats were then examined after 8 days. Drug-free colitis control rats showed severe disease pathol. with significant mortality (39%). Rats pre or posttreated with the C5a antagonist (10 mg/kg/day peroral, 0.3 mg/kg/day s.c.) had reduced mortality and significantly improved macroscopic scores, colon edema, colon myeloperoxidase levels, reduced concns. of TNF- $\alpha$  levels in the colon and serum, and had greater food intake resulting in greater weight gains than colitis-only rats. Rats pretreated with prednisolone (1 mg/kg/day s.c.) displayed significant improvement in parameters measured, but posttreatment was ineffective. Single dose pretreatment with the TNF- $\alpha$  inhibitor infliximab (3 mg/kg i.v.) also had significant improvements in the parameters measured. Rats pretreated with a combination of the C5a antagonist and prednisolone showed no greater improvements than either drug alone. These findings suggest a central role for complement, particularly C5a, in the pathol. of TNBS-induced colitis in rats, indicating a possible therapeutic role for C5a antagonists in inflammatory bowel disease.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

N(2)-[(2,2-diphenylethoxy)acetyl]-L-arginine (C3aRA) has been compared with a C5a receptor antagonist (C5aRA), AcF-[OPdChaWR], in a rat model of intestinal I/R. C3aRA (IC<sub>50</sub> = 0.15  $\mu$ M) and C5aRA (IC<sub>50</sub> = 0.32  $\mu$ M) bound selectively to human polymorphonuclear leukocyte (PMN) C3a and C5a receptors, resp. Effects on circulating neutrophils and blood pressure in the rat were also assessed. Anesthetized rats, subjected to intestinal ischemia (30 min) and reperfusion (120 min), were administered i.v. with either (A) the C3aRA (0.1-1.0 mg kg<sup>-1</sup>); the C5aRA (1.0 mg kg<sup>-1</sup>); the C3aRA+C5aRA (each 1.0 mg kg<sup>-1</sup>); or vehicle, 45 min prior, or (B) the C3aRA (1.0 mg kg<sup>-1</sup>) or vehicle, 120 min prior to reperfusion. The C3aRA and C5aRA, administered 45 min prior to reperfusion, displayed similar efficacies at ameliorating several disease markers (increased edema, elevated ALT levels and mucosal damage) of rat intestinal I/R. The combination drug treatment did not result in greater injury reduction than either antagonist alone. However, doses of the C3aRA (0.01-10 mg kg<sup>-1</sup>) caused transient neutropenia, and the highest dose (10 mg kg<sup>-1</sup>) also caused a rapid and transient hypertension. The C3aRA (1.0 mg kg<sup>-1</sup>), delivered 120 min prior to reperfusion to remove the global effect of C3aRA-induced neutrophil sequestration, did not attenuate the markers of intestinal I/R, despite persistent C3aR antagonism at this time. C3aR antagonism does not appear to be responsible for the anti-inflammatory actions of this C3aRA in intestinal I/R in the rat. Instead, C3aRA-mediated global neutrophil tissue sequestration during ischemia and early reperfusion may account for the protective effects observed

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:292659 CAPLUS

DOCUMENT NUMBER: 141:16889

TITLE: Potent cyclic antagonists of the complement C5a receptor on human polymorphonuclear leukocytes. Relationships between structures and activity

AUTHOR(S): March, Darren R.; Proctor, Lavinia M.; Stoermer, Martin J.; Sbaglia, Robert; Abbenante, Giovanni; Reid, Robert C.; Woodruff, Trent M.; Wadi, Khemar; Paczkowski, Natalii; Tyndall, Joel D. A.; Taylor, Stephen M.; Fairlie, David P.

CORPORATE SOURCE: Institute for Molecular Bioscience, University of Queensland, Brisbane, Australia

SOURCE: Molecular Pharmacology (2004), 65(4), 868-879  
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:16889

AB Human C5a is a plasma protein with potent chemoattractant and pro-inflammatory properties, and its overexpression correlates with severity of inflammatory diseases. C5a binds to its G protein-coupled receptor (C5aR) on polymorphonuclear leukocytes (PMNLs) through a high-affinity helical bundle and a low-affinity C terminus, the latter being solely responsible for receptor activation. Potent and selective C5a antagonists are predicted to be effective anti-inflammatory drugs, but no pharmacophore for small mol. antagonists has yet been developed, and it would significantly aid drug design. We have hypothesized that a turn conformation is important for activity of the C terminus of C5a and herein report small cyclic peptides that are stable turn mimics with potent antagonism at C5aR on human PMNLs. A comparison of solution structures for the C terminus of C5a, small acyclic peptide ligands, and cyclic

INVENTOR(S): Harkin, Denis W.; Lindsay, Thomas F.; Taylor, Steven  
 PATENT ASSIGNEE(S): The University of Queensland, Australia  
 SOURCE: PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100975	A1	20041125	WO 2004-AU642	20040514
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004238089	A1	20041125	AU 2004-238089	20040514
EP 1635857	A1	20060322	EP 2004-732886	20040514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.:			AU 2003-902354	A 20030515
			WO 2004-AU642	W 20040514
OTHER SOURCE(S): MARPAT 141:420440				
AB The invention discloses methods for treatment of hemorrhagic shock, and especially to treatment of this condition with cyclic peptidic and peptidomimetic compds. which have the ability to act as antagonists of the C5a receptor. In one embodiment, the compds. are active against C5a receptors on polymorphonuclear leukocytes and macrophages. Particularly preferred compds. for use in the invention are disclosed.				
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				
L26 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN				
ACCESSION NUMBER: 2004:533081 CAPLUS				
DOCUMENT NUMBER: 141:235998				
TITLE: Comparative anti-inflammatory activities of antagonists to C3a and C5a receptors in a rat model of intestinal ischaemia/reperfusion injury				
AUTHOR(S): Proctor, Lavinia M.; Arumugam, Thiruma V.; Shiels, Ian; Reid, Robert C.; Fairlie, David P.; Taylor, Stephen M.				
CORPORATE SOURCE: School of Biomedical Sciences, University of Queensland, Brisbane, 4072, Australia				
SOURCE: British Journal of Pharmacology (2004), 142(4), 756-764				
CODEN: BJPCBM; ISSN: 0007-1188				
PUBLISHER: Nature Publishing Group				
DOCUMENT TYPE: Journal				
LANGUAGE: English				
AB Complement activation is implicated in the pathogenesis of intestinal ischemia-reperfusion injury (I/R), although the relative importance of individual complement components is unclear. A C3a receptor antagonist				

RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2004-901652 A 20040326

OTHER SOURCE(S): MARPAT 143:360125

AB This invention relates to the treatment of neurol. conditions with novel cyclic peptidic and peptidomimetic compds. which have the ability to modulate the activity of C5a receptors. The compds. preferably act as antagonists of the C5a receptor, and are active against C5a receptors on polymorphonuclear leukocytes, monocytes, lymphocytes and/or macrophages. In a preferred form of the invention the neurol. conditions are neurodegenerative diseases, neuroimmunol. disorders, diseases arising from dysfunction of the blood brain barrier, and stroke.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:237352 CAPLUS

DOCUMENT NUMBER: 142:423355

TITLE: A potent and selective inhibitor of group IIa secretory phospholipase A2 protects rats from TNBS-induced colitis

AUTHOR(S): Woodruff, Trent M.; Arumugam, Thiruma V.; Shiels, Ian A.; Newman, Michelle L.; Ross, Paul A.; Reid, Robert C.; Fairlie, David P.; Taylor, Stephen M.

CORPORATE SOURCE: School of Biomedical Sciences, Department of Physiology & Pharmacology, University of Queensland, Brisbane, QLD 4072, Australia

SOURCE: International Immunopharmacology (2005), 5(5), 883-892  
CODEN: IINMBA; ISSN: 1567-5769

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Secretory phospholipase A2 (sPLA2) enzymes have been implicated in the pathogenesis of human inflammatory bowel disease (IBD). In this study we compared the efficacy of a potent, new and highly selective inhibitor of group IIa human sPLA2 enzyme (5-(4-benzyloxyphenyl)-4S-(7-phenylheptanoylamino)-pentanoic acid; sPLA2I), with that of sulfasalazine, in a rat model of trinitrobenzene sulfonic acid (TNBS)-induced colitis. Following a single oral dose of sPLA2I (5 mg/kg), pharmacoeactive levels of drug were detected in the serum within 15 min and for up to 24 h by liquid chromatog. mass spectrometry anal. Rats treated with sPLA2I (5 mg/kg/day) prior to induction of colitis were significantly healthier than TNBS-alone rats, as shown by reduced mortality, improved food intake and increased body weight, and significantly reduced colon myeloperoxidase levels, edema, tumor necrosis factor- $\alpha$  levels, and colon macroscopic pathol. scores after 8 days. Rats pretreated with sulfasalazine (100 mg/kg/day) also had reduced disease expression markers similar to the sPLA2I, but exhibited no improvement in colon edema. This study supports a role for the group IIa sPLA2 enzyme in pathol. associated with the TNBS rat model of IBD, and suggests a possible therapeutic application for selective inhibitors of group IIa sPLA2 inhibitors in the treatment of IBD.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1015896 CAPLUS

DOCUMENT NUMBER: 141:420440

TITLE: Treatment of hemorrhagic shock using complement 5a receptor inhibitors

CORPORATE SOURCE: School of Biomedical Sciences, University of  
Queensland, St. Lucia, 4072, Australia  
SOURCE: Expert Opinion on Therapeutic Patents (2006), 16(4),  
445-458  
CODEN: EOTPEG; ISSN: 1354-3776  
PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

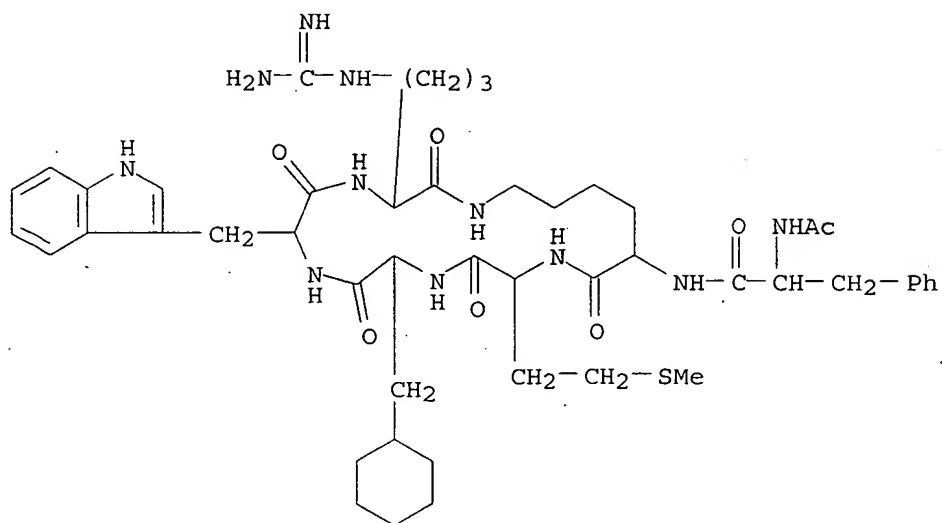
AB A review. Complement factor 5a (C5a) is formed upon complement system activation in response to infection, injury, or disease. While C5a is a potent mediator of immune and inflammatory processes, excessive production or inadequate regulation of C5a has been implicated in the pathogenesis of numerous immuno-inflammatory diseases, predominantly through exptl. studies utilizing animal models of disease. Both acute and chronic conditions may benefit from C5a inhibition, including rheumatoid arthritis, inflammatory bowel disease, asthma, psoriasis, hemorrhagic shock, and neurodegenerative conditions. The potentially broad clin. application for treatments that inhibit the activity of C5a at C5a receptors and the large global market for anti-inflammatory therapeutics have made C5a and the C5a receptor attractive targets for academic and com. drug development programs. In the past 5 years, interest in C5a as a drug target has grown substantially, and this activity has resulted in a collection of patents and scientific papers reporting novel C5a and C5a receptor inhibitors and antagonists, and generated a secondary stream of patent applications broadly claiming the use of C5/C5a inhibitors as a method of treating various immune and inflammatory conditions. This paper reviews the physiol. and pathophysiol. of C5a and discuss the development of C5a and C5a receptor inhibitors in light of the recent scientific and patent literature.

REFERENCE COUNT: 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L26 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

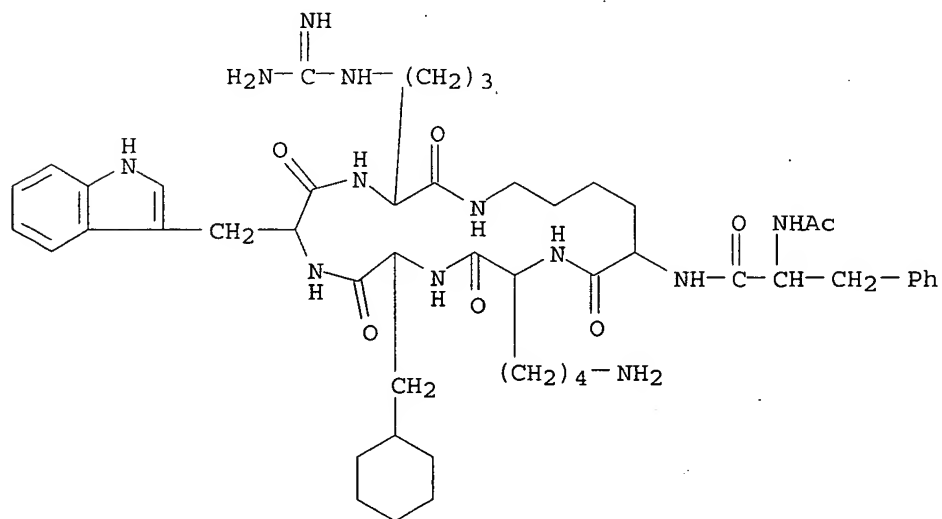
ACCESSION NUMBER: 2005:1075648 CAPLUS  
DOCUMENT NUMBER: 143:360125  
TITLE: Treatment of neurological conditions using complement  
C5A receptor modulators  
INVENTOR(S): Woodruff, Trent Martin; Taylor, Stephen  
Maxwell  
PATENT ASSIGNEE(S): Promics Pty. Limited, Australia  
SOURCE: PCT Int. Appl., 65 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092366	A1	20051006	WO 2005-AU403	20050321
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,			



RN 219639-79-9 CAPLUS

CN D-Arginine, N-acetyl-L-phenylalanyl-L-lysyl-L-lysyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:287477 CAPLUS

DOCUMENT NUMBER: 144:424981

TITLE: Recent developments in C5/C5a inhibitors

AUTHOR(S): Proctor, Lavinia M.; Woodruff, Trent M.; Taylor, Stephen M.



and therapeutic use)

IT Shock (circulatory collapse)  
(septic; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors; and therapeutic use)

IT Lupus erythematosus  
(systemic; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

IT 144554-94-9P 219639-70-0P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

IT 211937-00-7P 211937-01-8P 212054-79-0P 219639-69-7P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

IT 133009-92-4 157952-15-3 157952-23-3 177792-89-1 219639-68-6  
219639-71-1 219639-72-2 219639-73-3 219639-74-4 219639-75-5  
219639-76-6 219639-77-7 219639-78-8 219639-79-9  
219639-80-2 219639-81-3 219639-82-4 219639-83-5 219639-85-7  
219639-88-0 219639-89-1  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

IT 80295-54-1, Complement C5a  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

IT 219639-78-8 219639-79-9  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

RN 219639-78-8 CAPLUS

CN D-Arginine, N-acetyl-L-phenylalanyl-L-lysyl-L-methionyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)

- receptors, and therapeutic use)
- IT Anti-Alzheimer's agents
- Anti-inflammatory agents
- Anti-ischemic agents
- Antirheumatic agents
- Drug delivery systems
- Molecular modeling
- Multiple sclerosis
- Psoriasis
- Structure-activity relationship
- Transplant rejection
  - (cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Lipopolysaccharides
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
  - (cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Peptides, biological studies
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
  - (cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT **G protein**-coupled receptors
  - RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
  - (cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Peptides, biological studies
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
  - (cyclic; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Dialysis
  - (extracorporeal post-dialysis syndrome; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Gingiva
  - (gingivitis; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Lung, disease
  - Reperfusion
    - (injury; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Heart, disease
  - (ischemia; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors, and therapeutic use)
- IT Agranulocytosis
  - (neutropenia; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and **G protein**-coupled receptors,

L13 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:34926 CAPLUS

DOCUMENT NUMBER: 130:105315

TITLE: Cyclic agonists and antagonists of C5a receptors and G protein-coupled receptors

INVENTOR(S): Fairlie, David; Taylor, Stephen Maxwell; Finch, Angela Monique; Wong, Allan

PATENT ASSIGNEE(S): The University of Queensland, Australia

SOURCE: PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900406	A1	19990107	WO 1998-AU490	19980625
W: AU, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9880926	A1	19990119	AU 1998-80926	19980625
AU 744991	B2	20020307		
EP 1017713	A1	20000712	EP 1998-930536	19980625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508767	T2	20020319	JP 1999-505154	19980625
US 6821950	B1	20041123	US 2000-446109	20000421
PRIORITY APPLN. INFO.:			AU 1997-7550	A 19970625
			WO 1998-AU490	W 19980625

OTHER SOURCE(S): MARPAT 130:105315

ED Entered STN: 19 Jan 1999

AB Cyclic compds. are provided which have the ability to modulate the activity of G protein-coupled receptors. The invention provides both agonists and antagonists. In preferred embodiments, the invention provides cyclic peptidic and cyclic or non-cyclic non-peptidic antagonists or agonists of C5a. The compds. of the invention are both potent and selective, and are useful in the treatment of conditions mediated by G protein-coupled receptors, especially conditions mediated by overexpression or underregulation of C5a, such as a variety of inflammatory conditions.

IC ICM C07K007-06

ICS C07K007-64; A61K038-08

CC 1-7 (Pharmacology)

Section cross-reference(s): 63

ST cyclic agonist antagonist G protein coupled receptor;

C5a receptor cyclic agonist antagonist; peptide cyclic agonist antagonist

C5a receptor; antiinflammatory C5a receptor cyclic agonist antagonist

IT Complement receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process).

(C5a; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

IT Respiratory distress syndrome

(adult; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled receptors, and therapeutic use)

IT Antiarteriosclerotics

(antiatherosclerotics; cyclic peptidic and nonpeptidic agonists and antagonists of C5a receptors and G protein-coupled)

350850-77-0 350850-79-2 350850-81-6 350850-83-8 350850-85-0  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (melanin-concentrating hormone-related peptide ligand structure-activity relationships at human melanin-concentrating hormone receptor SLC-1)

IT 350849-88-6

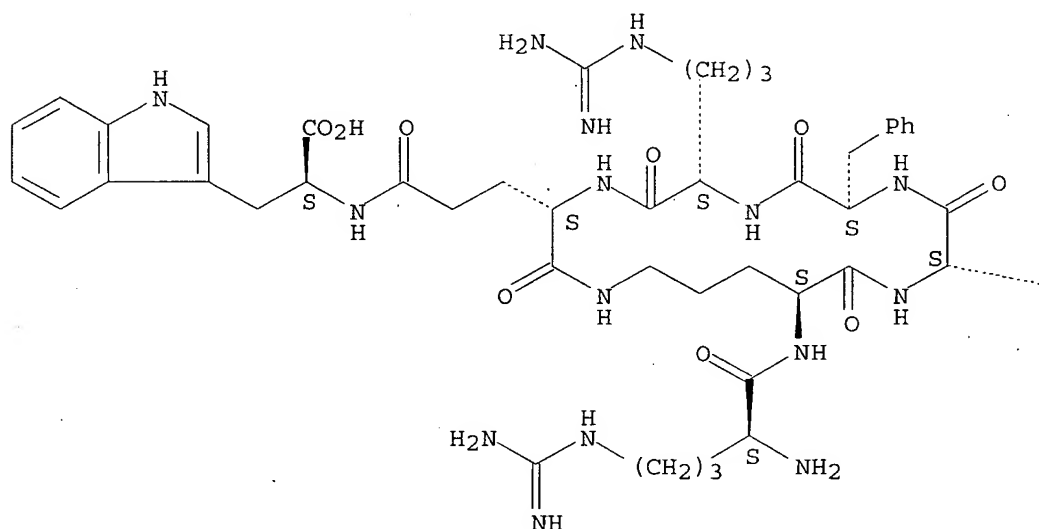
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (melanin-concentrating hormone-related peptide ligand structure-activity relationships at human melanin-concentrating hormone receptor SLC-1)

RN 350849-88-6 CAPLUS

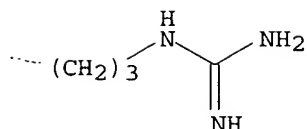
CN L-Tryptophan, L-arginyl-L-ornithyl-L-arginyl-L-phenylalanyl-L-arginyl-L- $\gamma$ -glutamyl-, (6-2)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

514814-87-0P 514814-88-1P 514814-89-2P 514814-91-6P 514814-92-7P  
 514814-93-8P 514814-94-9P 514814-95-0P 514814-96-1P 514814-97-2P  
 514814-98-3P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cyclic peptides and peptidomimetic compds. as G  
**protein-coupled receptor antagonists, and therapeutic use)**

IT 514814-55-2 514814-69-8 514814-70-1 514814-78-9  
 514814-79-0 514814-99-4

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclic peptides and peptidomimetic compds. as G  
**protein-coupled receptor antagonists, and therapeutic use)**

IT 514815-01-1 514815-02-2 514815-04-4

RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)  
 (cyclic peptides and peptidomimetic compds. as G

**protein-coupled receptor antagonists, and therapeutic use)**

IT 514815-00-0P 514815-03-3P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cyclic peptides and peptidomimetic compds. as G  
**protein-coupled receptor antagonists, and therapeutic use)**

IT 514814-39-2P 514814-40-5P 514814-41-6P 514814-48-3P 514814-50-7P

514814-53-0P 514814-56-3P 514814-59-6P 514814-61-0P

514814-64-3P 514814-82-5P 514814-90-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(cyclic peptides and peptidomimetic compds. as G

**protein-coupled receptor antagonists, and therapeutic use)**

IT 514814-52-9P 514814-54-1P

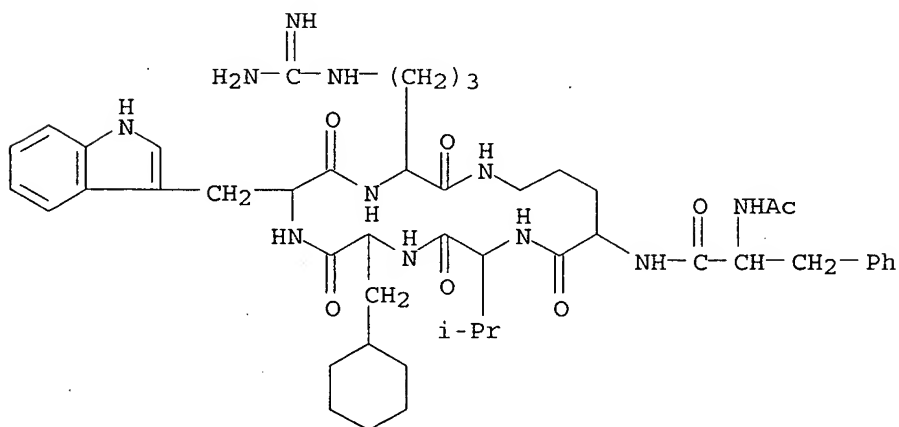
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cyclic peptides and peptidomimetic compds. as G

**protein-coupled receptor antagonists, and therapeutic use)**

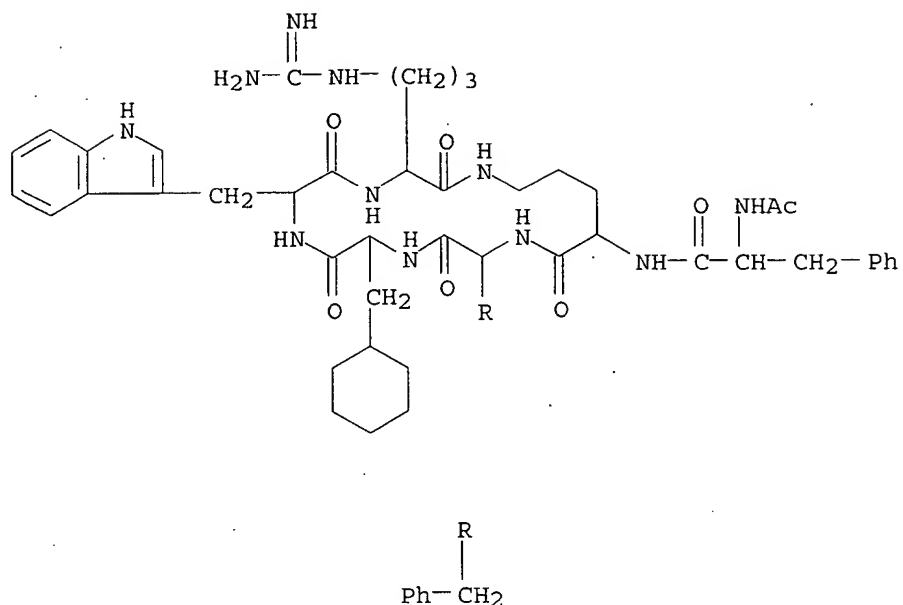
RN 514814-52-9 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-valyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)



RN 514814-54-1 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-phenylalanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)



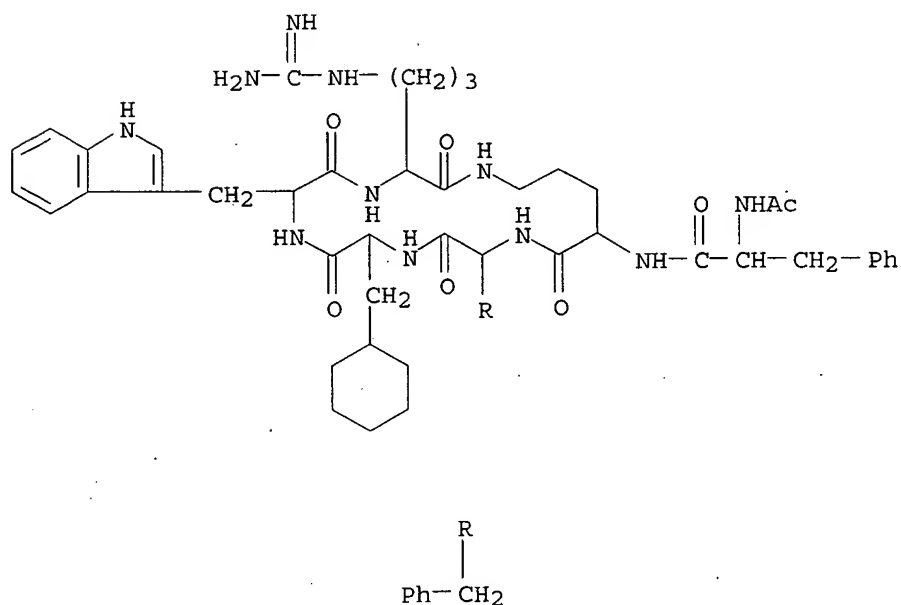
IT 514814-55-2

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclic peptides and peptidomimetic compds. as G protein-coupled receptor antagonists, and therapeutic use)

RN 514814-55-2 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-D-phenylalanyl-3-cyclohexyl-D-alanyl-L-tryptophyl-, (6→2)-lactam (9CI) (CA INDEX NAME)

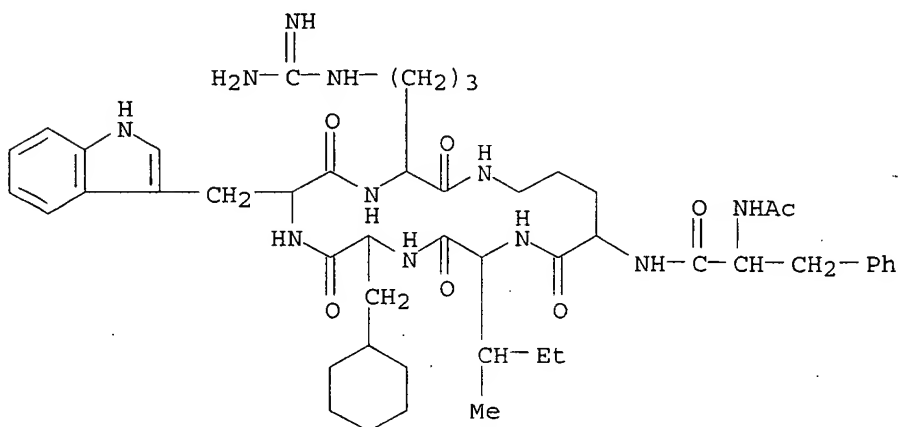


IT 514814-53-0P 514814-56-3P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(cyclic peptides and peptidomimetic compds. as G  
protein-coupled receptor antagonists, and therapeutic use)

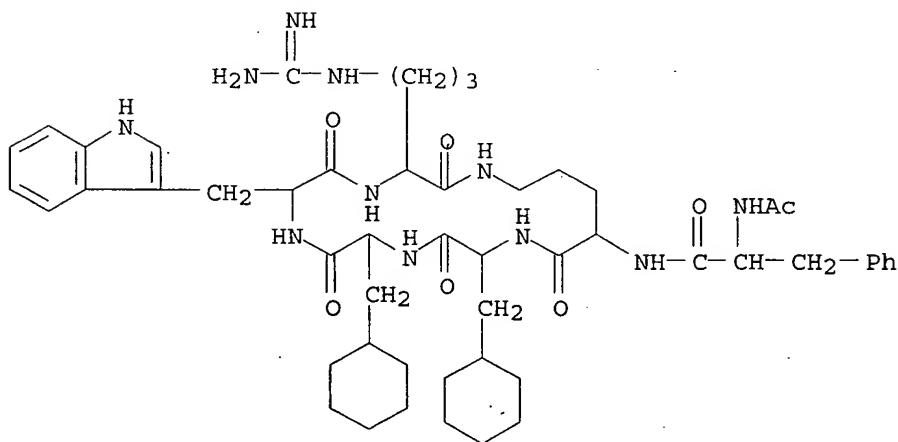
RN 514814-53-0 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-L-isoleucyl-3-cyclohexyl-D-  
alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX NAME)



RN 514814-56-3 CAPLUS

CN L-Arginine, N-acetyl-L-phenylalanyl-L-ornithyl-3-cyclohexyl-L-alanyl-3-  
cyclohexyl-D-alanyl-L-tryptophyl-, (6-2)-lactam (9CI) (CA INDEX  
NAME)



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:329752 CAPLUS

DOCUMENT NUMBER: 135:117301

TITLE: Structure-activity relationship studies of  
melanin-concentrating hormone (MCH)-related peptide  
ligands at SLC-1, the human MCH receptor

AUTHOR(S): Audinot, Valerie; Beauverger, Philippe; Lahaye,

Chantal; Suply, Thomas; Rodriguez, Marianne; Ouvry, Christine; Lamamy, Veronique; Imbert, Jerome; Rique, Herve; Nahon, Jean-Louis; Galizzi, Jean-Pierre; Canet, Emmanuel; Levens, Nigel; Fauchere, Jean-Luc; Boutin, Jean A.

CORPORATE SOURCE: Division de Pharmacologie Moleculaire et Cellulaire, Institut de Recherches SERVIER, Croissy sur Seine, 78290, Fr.

SOURCE: Journal of Biological Chemistry (2001), 276(17), 13554-13562

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 09 May 2001

AB Melanin-concentrating hormone (MCH) is a cyclic nonadecapeptide involved in the regulation of feeding behavior, which acts through a G protein-coupled receptor (SLC-1) inhibiting adenylyl cyclase activity. In this study, 57 analogs of MCH were investigated on the recently cloned human MCH receptor stably expressed in HEK293 cells, on both the inhibition of forskolin-stimulated cAMP production and guanosine-5'-O-3-[35S]thiotriphosphate ([35S]GTPγS) binding. The dodecapeptide MCH-(6-17) (MCH ring between Cys7 and Cys16, with a single extra amino acid at the N terminus (Arg6) and at the C terminus (Trp17)) was found to be the minimal sequence required for a full and potent agonistic response on cAMP formation and [35S]GTPγS binding. We Ala-scanned this dodecapeptide and found that only 3 of 8 amino acids of the ring, namely Met8, Arg11, and Tyr13, were essential to elicit full and potent responses in both tests. Deletions inside the ring led either to inactivity or to poor antagonists with potencies in the micromolar range. Cys7 and Cys16 were substituted by Asp and Lys or one of their analogs, in an attempt to replace the disulfide bridge by an amide bond. However, those modifications were deleterious for agonistic activity. In [35S]GTPγS binding, these compds. behaved as weak antagonists (KB 1-4 μM). Finally, substitution in MCH-(6-17) of 6 out of 12 amino acids by non-natural residues and concomitant replacement of the disulfide bond by an amide bond led to three compds. with potent antagonistic properties (KB = 0.1-0.2 μM). Exploitation of these structure-activity relationships should open the way to the design of short and stable MCH peptide antagonists.

CC 2-2 (Mammalian Hormones)

IT G protein-coupled receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(SLC-1; melanin-concentrating hormone-related peptide ligand structure-activity relationships at human melanin-concentrating hormone receptor SLC-1)

IT 87218-84-6, Melanin-concentrating hormone (Oncorhynchus keta)

128315-56-0, Melanin-concentrating hormone (human) 160201-86-5

350849-83-1 350849-84-2 350849-85-3 350849-86-4 350849-87-5

350849-88-6 350849-89-7 350849-90-0 350849-91-1

350849-93-3 350849-95-5 350849-97-7 350849-99-9 350850-01-0

350850-03-2 350850-05-4 350850-07-6 350850-09-8 350850-11-2

350850-13-4 350850-15-6 350850-17-8 350850-19-0 350850-21-4

350850-23-6 350850-25-8 350850-27-0 350850-29-2 350850-31-6

350850-33-8 350850-35-0 350850-37-2 350850-39-4 350850-41-8

350850-43-0 350850-45-2 350850-47-4 350850-49-6 350850-51-0

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350850-66-7 350850-68-9 350850-71-4 350850-73-6 350850-75-8